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Pharmaceutical Entry and Exit:

Evidence from a Reference Price Reform

Master's Thesis
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Abstract

In this thesis I study the impact of pharmaceutical reference pricing on the entry/exit of firms. I study how the adoption of reference pricing in Finland affected market competition and firm behaviour. I have a particularly rich panel data set on package-level sales by chemical ingredient in the Nordics from 2006-2013. As I am able to perfectly match chemical ingredients across different Nordic countries, I am able to control for country-specific variation in the sales of chemical ingredients, that occurred unrelated to the policy reform.

I use a differences-in-differences Poisson regression as my main empirical set-up and find only very limited evidence, that the price control policy would have had any effect on firm entry. Using Denmark as a control group I find that reference pricing decreased growth in the number of firms by 0-8%, but this effect dissipates when adding Norway as an additional control group, suggesting that the results are not robust. I find no effect on branded or generic pharmaceutical firms, but a limited, statistically significant negative effect on parallel importing firms.

Keywords Reference Pricing, Health Economics, Industrial Organization, Static Entry Models

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Abstract of master's thesis

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Tiivistelmä

Tässä opinnäytetyössä tarkastelen, miten lääkemarkkinoilla toimiva viitehinnoittelu on vaikuttanut yrityksien toimintaan markkinoilla. Tarkastelun kohteena on se, miten Suomen viitehintasääntelyn käyttöönotto vuonna 2009 vaikutti yrityksien markkinoille tuloon ja sieltä poistumiseen. Käytössäni on ollut laaja Pohjoismainen lääkemyyntiaineisto vuosilta 2006-2013, jota hyödynnän tarkastelussa. Koska pystyn tarkasti tunnistamaan samojen kemiallisten yhdisteiden markkinarakenteet yli maiden, pystyn kontrolloimaan näiden yhdisteiden markkinarakenteiden muutoksia. Tällöin pystyn laskemaan tarkasti, miten viitehintasääntely on vaikuttanut lääkemarkkinoiden kilpailuun Suomessa.

Käytän ns. differences-in-differences Poisson-menetelmää pääasiallisena analyysityökalunani. Löydän vain epäsuoraa todistusta, että kyseisellä hintamekanismilla olisi ollut mitään vaikutusta markkinarakenteeseen Suomessa. Yrityksien lukumäärän kasvu oli Suomessa enimmillään mittaluokkaa 0-8% pienempää kuin Tanskassa, mutta nämä tulokset eivät olleet robusteja. Havaitsin kuitenkin tilastollisesti merkittävän tuloksen rinnakkaistuontiyrityksille, eli viitehinnoittelulla on voinut olla negatiivinen vaikutus rinnakkaistuontiyrityksien markkinoille tuloon Suomessa.

Avainsanat Viitehintasääntely, Taloustiede, Toimialan taloustiede, Terveystaloustiede

Contents

1 Introduction

Forms of reference pricing have been used in the Nordic pharmaceutical markets for nearly three decades now. The short-run price decreasing effects from adopting the policy are well documented (see Matteo, Miraldo, and Ghislandi (2011) or Lopez-Casasnovas and Puig-Junoy (2000)). Reference pricing clusters drugs based on some equivalence criteria and sets a maximum reimbursement rate, usually based on the cheapest price or average price of the group. This reimbursement cap incentives consumers to choose cheaper versions of the same drugs, thereby inducing cost-savings for the public health care sector. As national health services are chronically trying to contain rising health care expenditures, often driven by aging populations, the appeal of reference pricing is easy to see.

In order to gain a holistic view of reference pricing as a policy tool, we need to understand the policy's long-run effects on innovation, market structure and prices. In this thesis I will focus on studying the impact of pharmaceutical reference pricing on market structure in order to study if the decreased prices cause fewer entrants or if reference pricing induces the entry of lesser known brands. Relatively few studies (i.e. Brekke, Holmas, and Straume (2011) or Kaiser, Mendez, and Rønde (2010)) have addressed this question, but it carries significant weight as market competitiveness has direct implications on both firm and consumer welfare. I study market competition through firm entry and exit utilizing empirical industrial organization models as the primary toolkit for my analysis. Firm entry is generally considered to be a key channel through which competition occurs, therefore empirically studying firm entry is often used to model market structure and competition and it has it's own rich body of literature which I will discuss in this thesis.

By accessing a particularly rich data-set that covers pharmaceutical sales and

prices in the Nordics and by using the implementation of reference pricing in 2009 in Finland as a source of exogenous variation, I am able to elicit information of the long-run effects that reference pricing had on firm entry and exit. I have product-level panel data from Finland, Denmark and Norway from the years 2006-2013. I use a cross-country Poisson diff-in-diff model to study this question and I am able to perfectly match the same pharmaceutical chemical substances across countries, which allows me to credibly control for exogenous variation that occurred unrelated to the policy reform. Therefore I believe my results accurately capture firm behavior in response to the policy reform.

In this thesis I will present a brief overview of reference pricing literature both from an institutional and theoretical standpoint. I will describe the pharmaceutical regulation and market structure of Finland and Denmark, which I use as my primary control group. The final chapters of this thesis are reserved for the empirical analysis where I employ a diff-in-diff Poisson-regression to study the impact that reference pricing had on entry into the Finnish pharmaceutical market.

2 The Finnish Pharmaceutical Legislation

Finland introduced mandatory generic drug substitution in 2003, which legally required pharmacies to inform consumers if cheaper versions of their prescription drugs were available. Drug interchangability is determined through substitution groups which are pools of similar drugs and are determined by the Finnish Medicines Agency, henceforth known as Fimea. A substitution group consists of drugs which are "comparable", meaning that the drugs have the same chemical active ingredient, strength and package size.[1] Essentially the idea is to replace a more expensive version of the drug, often the originator or “branded drug", with a cheaper version of the drug that offers the same therapeutic properties. In rarer cases, substitution groups can also be constructed from drugs that don’t have the same active ingredient if it has been established that the two distinct chemical ingredients have the same clinical effect, and this is known as therapeutic substitution.

Consumers had the right to refuse drug substitution without it affecting their reimbursement levels when generic substitution was first introduced in 2003. This reform was later supplemented by the introduction Reference Pricing in 2009, which imposes costs on consumers refusing drug substitution. If a drug belongs to a substitution group, meaning that the drugs offer the same efficacy, and the drugs have received a Reimbursement Status, then the drugs are chosen to form a reference price group. In the original reform it was also mandatory to have at least one generic producer in a reference group. Patented drugs are by default excluded from the reference price system as the patent provides market exclusivity so there are no comparable drugs from which to construct a reference price group. However, there are some exceptions to this rule: if the patent holder would’ve licensed the sale of

[1] Finnish Medicines Act 80/2003

their product to a competitor while simultaneously producing the drug in the same market, theoretically the reference price would be formed as now there would be a comparable drug.

A Reimbursement Status must be applied separately for from The Pharmaceutical Pricing Board (Hila), for each individual package and a positive reimbursement status means that consumers are able to receive compensation for their prescription drugs from The Social Insurance Institution (Kela). The reference groups are constructed if all of the three criterion are full-filled: the drugs form a substitution group, the drugs are reimbursable and there is at least one generic drug within the reference group.[2]

The original legislation was revised in 2017, after which parallel imported drugs and branded drugs can form a substitution groups.[3] A parallel imported drug is a drug imported from an ETA-country. Parallel importing firms are arbitreurs that do not manufacture drugs themselves, rather they buy drugs from wholesalers which they then export from a lower price level EU country to a high price level EU country. Parallel import firms require market authorizations from regulators to import, but they do not require permission from the original producers of the drugs, as free movement of goods and services is protected in the EU (Maskus (2000)). Since parallel imported drugs are included in substitution groups, it means that patented drugs can be included in reference price groups, without the explicit consent of the original producer. In this scenario the branded and patented drug faces competition from its own products sold by a third party that has imported the drug from an ETA-country with a cheaper price level.

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[2] Finnish Health Insurance Act 802/2008

[3] Finnish Medicines Act 2016/1101

Once the reference price groups have been formed, Kela will compensate the drug purchases based on the cheapest price within the group. This cheapest price will determine the maximum compensation that the consumer will receive. When the price of the cheapest drug has been set a copayment is added on top, which is the true maximum reimbursement. In 2009, the price corridor was 1,50 for drugs that cost less than 40 euros and 2 euros for those above. For example, if the cheapest drug within a reference price group costs 35 euros, the total maximum reimbursement is 35+1.5 euros=36.5 euros. The price corridor was narrowed to 0,5 euros in 2017.[4] Companies are allowed to change their prices twice a month, while the reference prices and substitution groups are set 4 times a year. This leaves some leeway for firms to decide their pricing strategy.

Certain drugs might have conditional reimbursability based on the disease they are prescribed to.[5] For instance, a number of epilepsy drugs have a further medical use to treat other neurological conditions such as neuropathic pain on bipolar disorders. A consumer buying a drug to treat epilepsy will receive no reimbursement, while a consumer buying the very same drug to treat neuropathic pain will have their entire costs of purchase compensated. For some drugs, the compensation might equal the price of the drug while for others it could be a fraction of the price. In practice, this means that different products are subject to the reform at different intensities, but whether or not this will have a significant heterogeneous impact on firm behaviour is unclear.

In Finland, if the annual expenditure for reimbursable drugs exceed 600 euros then the out-of-pocket payments for any future purchases will only be a small nomi-

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[4] Finnish Medicines Act 1101/2016

[5] see for instance Finnish Govenment Decree 1149/2016

nal transaction fee.[6] This means that once the cap has been reached the demand of consumers will be virtually inelastic as they have no personal incentives to minimize the costs of pharmaceuticals. In theory such a consumer will be indifferent between choosing a cheaper generic drug or an expensive branded drug.

In comparison to other Nordic countries, Finland adopted the reference price policy relatively late. Denmark was the first to adopt the policy in 1993[7], Sweden soon followed and Norway adopted reference pricing in the early 2000's.[8] However, there are huge caveats when comparing the regulation across countries. For instance in Sweden, a "product of the month" is chosen from a substitution group, which needs to be in supply for all pharmacies accross Sweden. The product of the month's price is the reference price to which all other products' prices are compared to. Consumers will have the smallest out-of-pocket expense if they choose the product of the month or an equivalently priced product.[9] A list of the products of the month changes every month and the system has it's own institutional intricacies, yet it is still known as internal reference pricing.

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6 Health Insurance act 1319/2018 and Health Insurance Act 252/2015

7 Danish Public Health Insurance Act, 1138/1993

8 Norwegian Pharmacies Act 39/2000

9 Swedish Act on Pharmaceutical Benefits, 160/2002

3 Finnish vs. Danish institutions

In this section I will be discussing the differences in the competitive environment of the pharmaceutical sector in Finland and Denmark. As I am using the Danish market as a counterfactual to the Finnish market in my empirical set-up, it is important to understand how comparable the two markets truly are. In particular, local shocks in either country that are unrelated to the Finnish policy reform could violate the analysis, thus I will try and map all potential threats to validity that stem from institutional difference.

3.1 Danish reforms

Denmark was the first Nordic country to implement several of the cost-containment policies, which were later adopted by it's neighboring countries. In 1991 Denmark introduced voluntary generic substitution, whereby doctors were able to prescribe the generic counterparts of branded drugs to consumers.[10] Doctors would write a small G for prescriptions where they felt generic drugs were equivalent in quality with branded drugs, which is why the policy instrument is more familiarly known as the "G-Scheme". The policy procedure had only small success as doctors were initially hesitant to prescribe generics and consumers were even more hesitant to buy them even if they were available.

In part due the low uptake of the G-scheme policy, Denmark introduced internal reference pricing in 1993, once again being the first Nordic country to implement the policy.[11] In order to encourage price competition and to counteract possible

[10] BEK nr 710, 23/10/1991

[11] LOV nr 1138, 22/12/1993

limitations in the expertise of doctors regarding drug safety, the Danish Ministry of Health changed voluntary substitution into mandatory substitution in 1997.[12] When prescribing medicines, doctors had to expressively opt out and forbid generic substitution rather than expressively permit drug substitution as in the G-scheme.

From 2000-2005, Denmark briefly experimented with external reference pricing, switching back to internal reference pricing in 2005.[13] As Denmark readopted internal reference pricing in 2005, the main analysis in this thesis isn't a before-and-after analysis of a country adopting reference pricing for the first time, using a country that never adopts the policy as a control group. Rather, it is a comparison between a country with stringent price control policies in place and a country adopting reference pricing for the first time.

When drawing conclusions from the analysis we assume that the competitive landscape of the Danish market had reached it's competitive equilibrium by 2006, which is the first year in the sample. The level of competition is irrelevant, only the fact that these policies don't increase or decrease competition at an accelerating rate during the period of interest. In particular, we assume that the switch from external reference pricing to internal reference pricing had no latent effects on the Danish market structure in 2006.

Finally, Denmark has deregulated the sale of Over-The-Counter (OTC) drugs, henceforth known with the acronym OTC, in 2001.[14] OTC-drugs are substances that consumers can buy without a prescription, such as many flu-medicines or weaker pain medications. In deregulated markets OTC-drugs can generally be bought from pharmacies and licensed supermarket outlets alike. The OTC-market represents

[12] BEK nr 308, 06/05/1997
[13] LOV nr 1431 af 22/12/2004
[14] LOV nr 493, 07/06/2001

roughly 10% of the sales in Finland and correspondingly roughly 10% of my sample. Finland has not deregulated it's OTC-drugs; OTC-drugs can only be sold in pharmacies with the exception of nicotine products, which were deregulated in 2006 in Finland and can be bought from many supermarkets or general stores.

3.2 EU-membership

Both Finland and Denmark belong to the EU and abide by the EU legislation. The EU has issued several directives that concern the pharmaceutical industry, from the safety standards of drug manufacturing to the longest acceptable period for market authorization applications' approvals by national agencies, and these directives apply to all EU member states. This should in theory prevent member states in setting up protectionist entry barriers for foreign firms, which means that firm entry should be a function of market conditions and firm productivity rather than arbitrarily set national rules.

In addition to manufacturing and entry regulations, the EU has attempted to harmonize patent regulation across the EU throughout the early 2000's (see for instance Directive 2001/83/EC or Regulation 726/2004/EC). Historically there have been differences in patent regulations between countries. Finland didn't allow for pharmaceutical substances or nutrients to be patented until 1995, opting instead for so called analogy process patents where the manufacture process of a pharmaceutical is patented, not the substance itself. In 1995 Finland joined the EU and the TRIPS agreement on intellectual property rights was drafted, both which affected Finnish pharmaceutical regulation. According to Cockburn, Lanjouw, and Schankerman (2016), since the 2000's patent regimes across the EU have converged towards the "TRIPS standard" while there was considerable heterogeneity in patent regulation in the previous decades. This means that patents for chemical ingredients should

expire at around the same time in the EU, which is important for the credibility of the analysis, as this would imply that potential entry would occur at the same time. However, it is important to note that no EU-wide patent exists and it is still up to the consideration of a originator firm to decide when and where it enters with it's patented products.

The majority of new chemical formulations need to apply for market approval through the European Medicines Agency (EMA), who assesses the scientific evidence, clinical trials, safety and efficacy of the chemical substances and grants market authorization for the applicant firms. A market authorization from the EMA will grant automatic approval in all EU member states, meaning that potential entry to both Finland and Denmark would occur simultaneously (European Medicines Agency (2018)).

For generic medicines, the process of market authorization is slightly different, as the safety and efficacy of a chemical substance has already been proven in clinical trials. Once the patent has expired, generic firms need to ensure that their product is of similar quality as those already in the market and that their manufacturing processes comply with regulation.

Generic medicines are generally encouraged to seek market authorization through national procedures, though it is possible to also apply centrally through EMA. Marketing authorization through a national procedure means that a drug manufacturer uses an existing market authorization in an EU country to seek further marketing authorizations in other EU countries (mutual recognition procedure) or simultaneously applies for market authorizations in a group of EU countries with a single application (decentralized procedure). In both national procedures, one EU countries' medicines agency takes the lead in reviewing the application and the national

procedures are generally less costly than the centralized procedure.[15]

Pricing and reimbursement are left to the discretion of each countries' regulatory bodies, which in turn means that there are discrepancies in pricing policies and firm profits between EU countries. Some of these price discrepancies are ameliorated by parallel trade, as large discrepancies should increase the profitability of arbitrage. However, as pricing and reimbursement regulation are unregulated at the EU-level, there are differences in price control policies between Finland and Denmark; although both countries have adopted similar policies such as generic substitution and internal reference pricing. In practice, for most prescription drugs sold in Denmark and Finland, the sales of the product begins when the product has received a positive reimbursement status, not when the market authorization application has been accepted.

3.3 Pharmaceutical Industry in Denmark

A key difference between the countries is that Denmark has a robust pharmaceutical industry, while the Finnish industry is dominated by one pharmaceutical company that contributes roughly 12% of all sales in Finland (Orion Oyj (2017)). In 2013, the Danish pharmaceutical market contributed roughly 2,6% of the Danish GDP which translated to roughly 12% of the goods exported. The market is dominated by three major companies, that combined contribute roughly 90% of the R&D done in Denmark and employ roughly 90% of headcount working in the Danish pharmaceutical industry (Copenhagen Economics (2016)).

As the pharmaceutical industry is such an important part of the Danish econ-

[15] Regulation 726/2004/EC

omy, this has lead to a rather unique system where The Danish Association of the Pharmaceutical Industry (Lif), which is a trade association representing the interest of pharmaceutical companies, is active in bilateral discussions with the regulatory agencies in Denmark. Lif has 39 members, that are mainly research based and that sell drugs in Denmark. Combined, it's members constituted roughly 60% of the revenue share in the retail market and 76% in the hospital sector and as such, Lif holds considerable decision making-power. (Hostenkamp (2011))

For instance, in 2001, 2006 and 2009 Lif voluntarily agreed with the Danish Ministry of Health to implement price ceilings for pharmaceutical products (Kaiser et al. (2010) and ISPOR (2015)). In 2006 these products included only reimbursable medicines while the 2009 price ceilings included all medicines. These agreements were binding for all Lif members and only a small amount of non-compliance occurred. These voluntary price ceilings coincided with some of the largest regulatory changes in the Danish pharmaceutical market: the deregulation of the OTC-medicines and the switch back from external reference pricing to internal reference pricing.

4 Literature Review

4.1 Reference pricing as a Policy Tool

The consumer could receive some utility from choosing a more expensive, branded drug if they perceive the quality of that drug to be higher or if they have specific brand preferences i.e. if consumers prefer drugs that were produced by small local producers rather than a multinational company's. Drug substitution is a commonly used tool to combat consumers quality misconceptions, as consumers may be unaware that the generic drug is indistinguishable from the branded drugs by their therapeutic properties. However, drug substitution on its own does not incentivize consumers who have reached their price cap to choose the cheapest drug as they have no personal interest to do so.

One of the main goals of the reference pricing is to affect the behaviour of the consumers that have reached their price cap as they are large cost drivers of public health care expenditure. These consumers may have expensive treatments or repeat purchases for a chronic illness. The reference price system creates a personal incentive for the consumer to purchase the cheapest possible drug and it sets a maximum reimbursement cap for the National Health Insurance. For some context, in Sweden in 2012 nearly half of the revenue from prescription pharmaceuticals was from patients who had reached their cost ceilings (Bergman, Granlund, and Rudholm (2012)).

The aim of the regulator is to affect consumer behaviour in such a manner that the consumers will minimize their own out-of-pocket drug expenditure and fiscal health expenditure simultaneously, without imposing any binding restrictions on consumers. Consumers are still able to buy drugs based on their individual

preferences, but they will have to pay for the difference between an expensive drug and the cheapest version of the drug in a substitution group from their own pocket.

The introduction of a reference price can impact pharmaceutical prices through a number of different channels. As different products are added into substitution and reference price groups, prices between the products become easier to compare. Uninformed consumers will receive more information for the true available basket of goods one might expect the prices to fall as a result of consumer switching from branded drugs to their generic counterparts. Price convergence can also occur as a change of producers' behaviour if they lower price as a response to the formation of a reference group. Producers might not want to deviate from the group average so the branded drugs would lower their prices if pinned to a reference group.

Interestingly there is empirical evidence that branded drugs raise their prices as a response to a new generic entrant, known as the generic paradox (Grabowski & Vernon, 1992). The reason being that the branded drugs positions themselves differently from the generic producers and aim to capture only the brand-conscious, higher willingness-to-pay portion of the market. A formation of a reference price group is not analogous to a new generic entrant, but the same logic could still apply. The branded drug could price itself at the high-end of the reference price group or opt out of the price corridor entirely in order to capture the brand-aware market segment.

It is also important to note that there are two distinct Reference Price Systems with different policy implications: The External Reference Price System (ERP) and the Internal Reference Price System (IRP). In an External Reference Price System, the maximum reimbursement of a drug is determined by a price index of similar drugs sold in a basket of countries. In an Internal Reference Price system, the maximum reimbursement is determined by the internal market i.e. by direct

competitors operating in the same country.

However, within the literature there is a clear lack of distinct terms as reference pricing can be used to describe both internal and external reference pricing, even though the two policies have drastically different implications. There is no set term of how an external reference price is calculated: averages, weighted averages and lowest list prices are all used in the EU-area (Carone, Schwierz, & Xavier, 2012). Some studies (i.e. Rémuzat et al. (2015)) find that Finland employs an external reference pricing scheme. This is because Hila determines a price-cap for wholesale prices for drugs that are reimbursable and uses the price-levels of other EU countries as a benchmark.[16]

One could argue that the system is closer to a bench-marking system or what is sometimes called Informal Reference Pricing, than a pure External Reference Price System; it aims to control for large deviations between Finnish prices and EU-level prices rather than set exact wholesaler price that would mirror EU averages. Wholesale prices of reimbursable drugs need to be approved by Hila, but below the limit there is still freedom for pharmaceutical companies to use their own consideration in pricing. In Finland, the reimbursement rates of drugs are not dependent on EU price-levels or reimbursement rates in other member states, therefore I would argue that Finland employs internal reference pricing with price-caps for reimbursable medicines rather than external reference pricing as suggested by Carone et al. (2012) and Rémuzat et al. (2015).

External reference pricing has been criticized because prices between different countries are generally not comparable (Toumi, Rémuzat, Vataire, and Urbinati (2014)). In practice, prices are affected by a country's reimbursement policy, by

[16] Health Insurance Act 1224/2004, Chapter 4

the amount of rebates paid by the drug manufacturers and by any number of unobservable qualities that are contingent on the country. When the international reference prices are directly applied to domestic pricing it can lead to severe market distortions. Pharmaceutical prices can end up below the levels of profitability, particularly if countries with high-volume sales are used in the reference basket, as those markets can afford to put lower prices in place, while less attractive markets with lower intrinsic sales volumes cannot.

Brekke et al. (2011) argued that an internal reference price system offers a higher incentive for domestic firms to reduce their prices as the reference price is endogenous. A producer's pricing scheme will affect the reference price in the following period and generic producers in particular will have a reinforced incentive to lower prices as they will receive a larger market share in the following period. Conversely, in an exogenous or external reference price system, any reduction in price will have no impact on the reference price in the following period. A producer who was already pricing below the external reference price will have an incentive to raise prices in the following period as their products will receive full reimbursement even with a higher price.

External reference price systems have also been criticized because of their spillover effects. Danzon, Wang, and Wang (2005) used the Cox proportional hazards model to estimate the time it took for a product that had received marketing authorization from the European Medicines Agency (EMA) to spread across the EU countries. The hazard rate is the entry time for a new product to appear in a market for the first time. An approval from EMA grants a market authorization to all EU countries, thus in theory the products could appear in all the markets simultaneously. However, the authors found that larger markets such as Germany had much shorter launch delays than smaller markets.

One proposed explanation for this is that producers fear that if they'd immediately introduce their products in smaller markets with lower price levels, such as Bulgaria, these products would be included in reference price baskets in countries such as Germany and the producers would cannibalize their own profits. The products could also be subject to parallel trade, meaning that arbitreurs would purchase cheaper version of the drugs sold in for example Bulgaria, repackage them and then sell them in Germany. Similar conclusions have been also reached by Kyle (2007) and more recently by Maini (2018).

Kyle (2007) argued that introducing price controls such as internal reference pricing will affect entry orders of new pharmaceuticals as firms have an incentive to enter markets where they can freely set higher prices, as this will allow them to set higher prices in countries with more stringent price controls. Using a similar strategy as Danzon, Kyle found that implementing price controls decreased the probability of entry by 75% when comparing to a country with no price controls. If launch delay is affected by the intensity of price controls in a country, then a valid concern is if the introduction of an internal reference pricing will influence market entry.

Industry representatives find that internal reference pricing is restrictive on incremental product development and that it diverts R&D expenditure into chemical substances where there is no reference pricing as there it is possible to freely set their prices (de Joncheere, Dukes, Haaijer-Ruskamp, and Rietveld (2003)). For therapeutic substitution the worry is that patients respond differently to molecular differences between the drugs. A system that would reward consumers only if they buy the cheapest drug in a basket even if the cheapest drug would cause adverse reactions for certain consumers, could be considered unfair.

Internal reference pricing isn't a traditional price control mechanism in the sense that it doesn't restrict firm behavior. Firms are still able to price their products

above the reference price freely: reference pricing only affects the reimbursement levels. Firms can also opt out of having reimbursable drugs in Finland after which they can price their products without any restrictions.

4.2 Reference Pricing on Firm Entry

Earlier empirical studies suggest that adopting a reference price system will have a moderate effect on prices, namely in the form of a price reduction. This effect has been documented by Koskinen (2018) in Finland, Pavcnik (2002) in Germany and Brekke et al. (2011) in Norway, with the results being ubiquitous. The effect on prices is anywhere between 10-30 percent (Galizzi et al. (2009)). However, the impact that reference pricing will have on entry is ambiguous.

As the out-of-pocket expenditure of consumers increases for products that are above the reference price, the incentives for consumers to by cheaper versions of drugs increase. For consumers that have no brand preferences, we move towards the elastic part of their demand curve as their budget constraint becomes more restrictive (Brekke, Konigbauer, and Straume (2007)). This additional constraint implies that the new optimal price for producers will be lower than the previous price which implies that overall profits will fall, ceteris paribus no increase in demand. For consumers that have brand preferences, where an increase in prices will not decrease demand, the generic paradox will occur. This occurs when a branded producer decides to raise prices in order to capture a larger portion of this market segment at the expense of the price elastic market segment. However, a relatively safe assumption is that overall market profitability will fall as the elastic consumers most likely outnumber those with strict brand preferences in most markets. Even if this is not the case and the brand conscious consumers were dominant, then the question is why producers wouldn't have increased profitability levels through higher

prices prior to reference pricing.

The decrease in profitability is exasperated by intensified price competition where firms undercut each other's prices by a marginal amount in order to secure a larger portion of the market share. Therefore, for some firms the regulation could result in profitability levels that wouldn't cover the marginal costs of production for a chemical ingredient, which would result in them dropping the product line. For others it could result in profitability levels that would fall below average costs, implying the firm could leave the entire domestic market as the revenue wouldn't be sufficient to cover the fixed costs of the operation any longer. In theory there should be a larger detrimental effect for the high-priced products, which are commonly branded products, as consumers are more price sensitive. Possible market entrants will search for greener pastures and inefficient producers will exit the market and the total effect of the policy reform on competition would be negative.

Reference pricing could therefore decrease the incumbent firms' ability to use market power; market power in this case could refer to a very established and well-known brand. Reference pricing would require consumers to pay a premium for their brand preferences, which could induce the entry of lesser known generic medicine producers. Both Brekke et al. (2011) and Kaiser et al. (2010) found a positive effect for the impact of reference pricing on generic entry. Brekke et al. find that reference pricing increased the number of generic firms by 1.245 firms while Kaiser et al. find that the quantity of packages sold by branded firms decrease after the introduction of reference pricing.

Kaiser et al. is particularly noteworthy for this thesis as it studies the introduction of reference pricing in Denmark. However, unlike most previous empirical literature where the interest has been on studying the implementation of reference pricing for the first time, the authors' paper studies Denmark's switch from exter-

nal reference pricing to internal reference pricing in 2005. Thereby, the authors aim to study how reference price design affects market outcomes such as pricing and quantities sold.

Kaiser et al. study the market of statins from 2003 to 2007 and they use a nested-logit model to estimate the demand for statins in Denmark. Nested-logit models are used to measure how product characteristics affect demand. Separate probabilities are calculated for consumers choosing characteristics that are orthogonal across local "nests", in this case across different statins, and for consumers choosing characteristics that are product-specific. Product-specific qualities that the authors used related to packaging, product names and firm names, implying that the Kaiser et al. were able to estimate the probability that a consumer purchases a branded product pre- and post-reform.

Reference pricing could have a heterogeneous impact based on firm type, as just discussed, but also by firm size. On the one hand, smaller firms with fewer product categories will not be able to cover fixed costs if the regulation impacts their key markets, in comparison to larger firms, that have multiple product lines and can cover fixed costs through a larger portfolio of products. On the other hand, large multinational firms need to consider sales in other European markets and might employ uniform pricing across markets. Therefore, small local producers that don't need to consider how their pricing affects sales in other markets are more agile with pricing and can adjust better to price competition, which can give them a competitive advantage.

As discussed in the previous section, heavy price controls could affect entry through the diffusion of products, as firms bring their products first to countries where there are less stringent price controls and where they can subsequently set a higher price (Kyle (2007)). In the EU, this is especially true as arbitrage from

lower price level countries to higher ones is permitted through parallel trade and many countries use external reference pricing, where they include other EU member states in the reference basket. Thus, firms could avoid smaller and cheaper countries entirely as not to cannibalize their own profits in more significant markets (see also Danzon et al. (2005) for more details).

When looking at therapeutic markets, firms could strategically select the markets in which they are present by avoiding those that are subject to harsher pricing policies and those markets where there are already a number of competitors present. An example of this is Scott-Morton (2000), who studied how certain market characteristics predicted generic entry. She studied markets that lost patent protection between 1986-1991, using the timing of patent expiration as the source of exogenous variation for market structure. Scott-Morton had data on the number of new drug applications submitted to the Food and Drug Administration (FDA) in the United States. She modelled the number of annual entries by a Poisson regression. She found that generic entry was positively predicted by revenue and if the drug was used to treat chronic illness while the number of subsequent entries decreased if the drug was an injectable drug or there already was a duopoly of firms present.

More recently, Moreno-Torres, Puig-Junoy, and Borrell (2009) studied the determinants of generic entry in the Spanish market. They used a negative binomial regression and studied how determinants such as the number of incumbent generic firms, the timing of a chemical ingredient being subject to reference pricing and the number of active ingredients at the ATC4-level affected further generic entry. The authors elicit information about the magnitudes of each determinant on future entry. For instance, the authors found that an increase of one generic incumbent decreased the probability of further expected entry by 2-5% and in comparison once a chemical ingredient was subject to reference pricing, the expected entry in the

subsequent period decreased by 8%. The authors do not have a credible control group which means that there could be Spain-specific unobserved shocks that affect all chemical groups simultaneously and by extension, the estimation results as well. Furthermore, there are some concerns over omitted variables: The number of incumbent firms and potential entrants in a chemical group are likely correlated and explained by any number of market characteristics.

This thesis is similar in spirit to both Scott-Morton and Puig-Junoy et al. as both heavily draw upon from the same earlier theoretical entry literature namely Bresnahan and Reiss and Ericson and Pakes (1995). In this literature, the number of entrants is modelled as a two-step decision process where first the firms decides whether or not to enter the market and in the the second step the firms compete and obtain pay-offs. One distinction is that I am not interested in evaluating the magnitudes of a matrix of market characteristics on generic entry; I am only interested on one determinant, which is the introduction of reference pricing on entry.

Empirically my set-up resembles also that of Yin (2008) who studies the impact of the 1983 Orphan Drug Act on the number of clinical trials in the US, which was a reform which offered incentives for pharmaceutical firms to develop drugs for rare diseases. Yin compares how the number of clinical trials changed between rare and non-rare diseases after the implication of the policy. Though the author does not model market structure, the empirical strategy is very similar as Yin attempts to study the effects of a policy change on the number of occurances (clinical trials) with a fixed-effects Poisson model using the Differeneces-in-differences method, which as I explain in the empirical section, is also the method I have chosen.

Reference pricing could have long-term effects not only on firm entry, but on innovation and the introduction of new chemical entities. These effects are difficult to empirically verify as the lags between the policy introduction and the change in

willingness' to innovate can be years if not decades (Abbott and Vernon (2007)). Therefore, this link is not studied in detail in this thesis. This is regrettable: calculating the net welfare effects of reference price policies would clearly require us to know what the long-term effects are on innovation.

In the results section I show that after the adoption of the reference price system, the share of generic packages grew faster in Finland than in the other Nordic countries. Though this is not causal nor inherently undesirable, it is still indicative that the competitive environment for off-patented products has become less favorable for originator products relative to generic drugs. In conclusion, the underlying conditions that affect companies' entry decisions are unknown. This research captures only a small component of those decisions, which is the indirect impact of price reductions caused by the adoption of the reference price system on entry.

5 Empirical Industrial Organization Entry Literature

In this section I will provide a brief overview of empirical industrial organization literature, when it is used and why traditional regression methods may be inadvisable to study market competition. Researchers rarely have detailed data on quantities or cost-functions, but there are several applications where inferences need to be made on both variables. For instance, a key research question of industrial organization and entry literature is to disentangle if the current market structure is a function of entry barriers or if it stems from superior production capabilities or first-mover advantages. This question has been extensively studied as it has concrete applications for antitrust policy and for firms planning their optimal levels of advertising, R&D, and strategic pricing.

The other difficulty that researchers face when trying to empirically study market behavior, is that there are several simultaneity issues. For instance, there are interdependencies between prices and quantities, there are interdependencies between market structure and profits; if one changes either variable the other variable is likely to follow suite. Therefore, trying to map these dependencies in a credible causal set-up requires it's own unique approach and literature, which I will present in this section.

The literature that I follow and will focus on most in this chapter, is the static entry literature. Static entry analysis in this case means that "entry" is more akin to "being active in the market" rather than "entering the market for the first time". I observe firms that entered, exited or were present in the market at a given time, but I will not be able to observe firms that could've entered the market, but chose not to do so. Furthermore, I do not have the tools to estimate the dynamic effects of entry:

how firms respond to entry decisions of their competitors in previous periods. In order to deal with this, I rely on some assumptions regarding the market dynamics, which are drawn from previous literature and, which I will discuss in further detail.

In several empirical static entry models firm actions are considered to be a two-step process where firms first decide if they want to be present in a give local market and then compete with prices. Local markets can refer to either geographic markets or product characteristics. For instance, a firm can choose to sell cereal, but can still segment their products by branding their product, changing the flavoring/recipe or altering the packaging. A local market in this case would represent each of these product characteristics separately and the hedonic effect different product characteristics have on price has it's own vast, separate sub-section of literature. In the pharmaceutical context, estimating product characteristics' effects on demand have been applied by for instance Bronnenberg, Dube, Gentzkow, and Shapiro (2015), who study the role of information in the demand of branded on non-branded pharmaceutical products.

In the static entry models, the firms' two-step decision process is influenced by the expected future profits which is a function of market size, the number of firms present and other observed market characteristics that influence either demand or cost-structures. Both market concentration and future profits are endogenous to firm behavior, as are R&D costs and future profits and this is an issue for causal inference, as you would need exogenous variation for either demand characteristics or firm choices.

In their seminal paper, Bresnahan and Reiss (1991) attempt to study how the variable profits of firms are influenced by entry and what is the role of fixed costs on the number of entrants. They divide fixed costs into exogenous and endogenous costs. Exogenous fixed costs are constant costs that all firms present in the market

have to incur that do not scale with operations, such as founding costs, administrative fees etc. whereas endogenous costs are investments that directly enable firms to "buy" market share such as the aforementioned Research and Development or advertising costs. The presence of endogenous fixed costs implies that there are returns to scale, meaning that it is entirely possible for incumbent firms to erect entry barriers. Using fixed sunk costs in order to model the "toughness of competition" is also a strategy that was explored by Sutton (1991), among others. In a series of papers during the 80's Sutton rigorously developed many of the same principals that were also used by Bresnahan and Reiss.

Bresnahan and Reiss use 202 small geographical US markets (towns) that are isolated i.e. entry decisions into separate markets aren't correlated with each other, in order to study what they call the "entry threshold". They define entry thresholds as the amount the market size must grow in order to induce the entry of another firm. Isolated markets also in this context also means that consumers don't switch across markets. The authors use the amount of population in these markets as a proxy for market size. Thus, entry threshold in the paper is the population increase required to accommodate a firm entry.

The strategy relies on the idea that potential market size is exogenous to the number of firms. The authors aren't able to regress the number of firms or entry on variable profits directly, as there is two-sided causality between the two: profits induce entry, while entry affects future profits. In order to solve this simultaneity bias, the authors proxy the entry of firms using potential market size. Their strategy relies on the assumption that firms are subject to a zero-profit condition: if the potential market size increases above the estimated entry threshold in later periods, then this will induce the entry of a new firm. Therefore, the authors are able to estimate how variable profits change with the entry of a new firm. The authors run

regressions using an ordered probit model as they allow for changes in the levels of entry thresholds, based on the number of firms already present. If the markets are highly contested, a constant increase in population might not be enough to induce the entry of a new firm. A key finding of the model was that the entry threshold converged very quickly after the number of firms in the market exceeded two firms. This implies that the competitive effects of an additional firm decreases rapidly if there are already two firms present.

A limitation of the original study is that the authors don't have accurate information on variable profits, rather they use qualitative data such as land-prices and income to estimate profits, which means that the regressions are sensitive to the changes in parameter specifications. Furthermore, the original study assumes that all firms are identical, which the authors acknowledge, but it means that the model doesn't take into account the effects of entry barriers or the effects that market changes have on different types of firms.

Because the Bresnahan and Reiss framework provides a tractable model that enables researchers to make inferences on fixed costs and demand with a limited amount of data, there have been several extensions of the model. For instance, Mazzeo (2002) has expanded on the original Bresnahan and Reiss-model by including a firm-quality indicator. Mazzeo is interested in studying how different type of producers compete and relaxes the homogenous firms condition in the original Bresnahan and Reiss paper.

In Mazzeo's model firms decide the markets in which they compete in but also their type. In the original paper he studied motels near highway exits and classified motels into "high" quality and "low" quality. Thus, a firm's decision matrix is the entry location and motel type. A similar categorization in the pharmaceutical industry could be done by defining firms as branded or generic firms. It should be

noted that this categorization is not necessarily a reflection of a product's quality, though it could be in the minds of some consumers.

Mazzeo's model allows for heterogenous firms to compete with one another. He assumes that additional market participants will have a more intensive competitive effect on their own type and variable profits decrease faster for the same firms, which suggests the existence of a competitive equilibrium. In the model the firms are still assumed to be homogenous within their subgroup, but the firm endogenizes it's own type decision. This enables Mazzeo to study how firm differentiation affects variable profits and demand.

As with Bresnahan and Reiss, Mazzeo assumes that firms make irreversible entry decisions where firms that enter the market face a fixed cost shock and those that have entered will make a positive profit and any marginal entrant would make a loss. The difference with Mazzeo's and Bresnahan and Reiss's papers is that in Mazzeo's paper firms are subject to two types of shocks: one's that affect the entire market and one's that affect firms with a similar typing.

Second, Mazzeo assumes that firms make entry decisions sequentially. This assumption guarantees the existence of a unique equilibrium. Sequential decision-making is a critical assumption. In Bresnahan and Reiss's a firm's choice set is a discrete enter/don't enter-decision and all firms are homogenous, meaning they have ex ante the same payoffs, but in contrast Mazzeo's model has an additional decision of firm type, which already creates the possibility of multiple Nash equilibriums. Sequential decision-making eliminates this problem, as a firm's choice set is a best response to what their competitor has already decided. There is still the issue of which firm's make the decisions first. This can be overcome by imposing additional assumptions, for instance assuming that the most profitable firm-types enter first. Mazzeo's results suggested a strong return to firm differentiation and his model pre-

dicts that similar firms would avoid each other in the market: the negative effect of a new entrant can be more than twice as large for firms of the same type according to Mazzeo. This negative effect can be outweighed by overall demand conditions as well and the overall demand conditions can predict both the number of firms overall and by type.

In both Bresnahan and Reiss' and Mazzeo's papers the number of firms in a market are summed and a decrease in this value would imply exit while an increase would imply entry. If we are interested in entry and exit, why not just run separate equations on entry and exit and then add the two results? The reason is that entry and exit are interdependent; in a market with high intensities of entry we assume that survival probability decreases as the entrants steal market-share and cut profits from the incumbents.[17] Entrants need to be at least as productive as the incumbents for entry to be profitable. Entry through radical innovation fundamentally disrupts the market and threatens firms. Therefore, we could except there to be more exit in markets with higher entry rates. Alternatively, we could argue that if producers see a market with a lot of growth potential, we could see a high intensity of entry without notable effects on exit.

If we want to estimate the total effects of a policy, the two-sided causation between entry and exit presents an empirical challenge, as we could not run two separate regressions and then simply sum the results due to the ambiguous dependence and confounding variables. There probably are omitted variables that predict both entry and exit such as the underlying beliefs about market conditions and market development. If the underlying omitted variables have an ambiguous effect on the error terms of the respective regression equations then the results would be biased

[17] Entry-exit's interdependence was empirically shown by Dunne, Roberts, and Samuelson (1988)

and even worse, the direction of this bias would be unclear.

The second underlying difficulty we face is that heterogeneous firms could reach any number of equilibria. If a policy such as reference pricing is successful in decreasing prices as intended by the policy maker, but as a by-product decreases profits as well, then the question is how should firms react to the new state? A firm exiting could mean that the remaining firms raise their prices near the original prices. If that's the case, then which firm should forgo future profits for the "common good" of their competitors? Once prices decrease is the appropriate response to invest and capture a larger portion of the market share or to refrain from investment precisely because the attractiveness of the market has decreased?

In the presence of multiple equilibrium, assuming that our empirical set-up was kosher and that the causal inferences would hold, then at best we could state that companies have moved from one equilibrium to another and we could infer that in the current equilibrium there has been more entry/less exit when compared with the previous dynamic equilibrium. In effect, this means that the external validity of the regression estimates is questionable since changing the context would drastically alter the results. The alternative approach would be to impose additional assumptions that may or may not be justified.

Both Mazzeo and Bresnahan and Reiss rely on strong assumptions regarding perfect information. They assume that firms perfectly observe each other's pay-offs. Most contemporary models (see i.e. Seim (2006), Toivanen and Waterson (2005) or more recently Grieco (2014)) have relaxed this assumption to include private information into the entry models, which allows for a more flexible description of the market. Relaxing the perfect information assumption allows the modelling of i.e. post-entry regret after the pay-offs are realized or firm's learning about market conditions through their competitors entry decisions. Perfect information is a

very strict condition, which reduces the applicability of models with this stringent requirement to accurately capture firm behavior.

Static entry models, though useful tools to measure competition and concentration, carry their own limitations. Several models have assumptions where potential entrants and incumbents are treated similarly, which negates the possibility to model firm or market history. More flexible and dynamic models have also been introduced that allow for more realistic depictions of real world firm behaviour. Dynamic models go outside of the scope of this thesis and will be left to the interest of the the reader.[18]

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[18] Examples of dynamic models include Pakes, Ostrovsky, and Berry (2007), Aguirregabiria and Mira (2007) and Dunne et al. (1988) among others.

6 Market Definition

Along with defining competition between producers, defining the scope of the market is the other critical choice a researcher must face. In this section I will briefly introduce the Anatomic Therapeutic Classification (ATC) System and explain the market definition that I will use in my empirical analysis. By far the most common way to define a pharmaceutical market in the previous literature is to use some Anatomical Therapeutic Chemical Classification or ATC-level as a market definition. The ATC-system is a method of classifying a drug based on it's active ingredient and pharmacological and chemical properties. The ATC-system is a classification system maintained by the World Health Organization and it has five distinct levels. Below we see an example of a sample product.

Table 1: ATC-levels of Heparin

Level	Definition	Code	Description
1	Anatomical Main Group	B	Blood and Blood Forming Organs
2	Therapeutic Sub-Group	B01	Antithrombotic agents
3	Pharmacological Sub-Group	B01A	Antithrombotic agents
4	Chemical Sub-Group	B01AB	Heparin group
5	Chemical Substance	B01AB01	Heparin

Heparin is a blood anticoagulant used in the treatment of heart attacks among other things as it has useful properties in preventing blood clotting. Note that in the case of Heparin, the Therapeutic and Pharmacological sub-groups are identical, but this need not be the case.

A common market definition in previous literature is to use either the ATC2 (i.e. Rudholm (2001)), or ATC5-level in the WHO-classification (see (Kyle, 2006) or Brekke et al. (2011)). The ATC2-level indicates the therapeutic subgroup, meaning

that the drugs in that level are roughly speaking used to treat the same diseases and it is the highest-level at which we expect substitution between the drugs to exist whereas the ATC5-level consists of products with the same active ingredient.

If the market definition is chosen at a very narrow level, then we expect that individual observations may be accurate, but we don't account for the presence of cross-substitution between the groups. Doctors often have a choice of what drug to prescribe for any given illness, but it is entirely possible that these choice-sets include drugs with different active chemical ingredients or pharmacological classifications.

Thus, if we only compare competition within the strictest market definition, e.g. defining the market as drugs with a certain chemical component, then we ignore the fact that in reality, the selected treatment method could be chosen from another set and the true outside option for the consumer is not only drugs with the same active ingredient, but drugs in other groups all together. The prices between these groups would be correlated as would the decisions to enter/exit the given market.

On the other hand, very general market definitions will provide very general results. The underlying heterogeneity in the market will be hidden within the aggregated results. Aggregating data into larger pools also decreases the amount of substitutability between the drugs, meaning that two distinct drugs in the same group might not be direct competitors as such. We would only see an aggregated average effect of the reform and the standard errors of the estimates will be very large as there would be a fewer number of observations. Due to this large amount of noise the model might not capture the true effect of the policy, should there even be one.

The optimal market definition depends on the research question and is influenced by the amount of data available. I have selected the ATC5-group as my relevant market, as it has identical products in the product characteristics space, thus the

products are local competitors. A benefit of this choice is that there are more ATC5-groups (266) compared to ATC2-groups (51) that were directly affected by the reference price reform. As a consequence my point estimates are more precise for ATC5-level estimates, though it means that I don't capture the entire effects of the reform as some competing products from other ATC5-groups not subject to the reform are omitted. This sample selection yields 266 unique chemical ingredient markets where I am able to study the effect of reference pricing.

7 Descriptive statistics

In this section I will provide some sample descriptive statistics on the Danish and Finnish pharmaceutical markets. The key question that I aim to answer is how representative Denmark is as a control group for Finland. As the focus of this thesis is on market structure, I will use indicators that elicit information on the competitiveness in each market.

The first indicator of competitiveness presented is a distribution of the Herfindahl-Hirschman Indices (HHI) within the two countries. The HHI measures the concentration of the market by summing the squares of market shares of the largest firms in the market. Typically HHI values of over 0.25 are considered highly concentrated, while values of 0.15-0.25 are considered moderately concentrated. I have calculated market shares per ATC5-group in a country and the ATC5-groups are narrowed to those that fall under Finnish reference pricing in 2009. This yields roughly 200 ATC5-groups or chemical ingredients for which a unique index-value is calculated. From these values we compile a distribution that reflects the variation in market concentration over time.

More formally, this can be presented as a matrix (T,I) where the elements t of a row (T) reflect the year and elements i of the column (I) reflect an HHI-value in a unique ATC5-group. This can be calculated by:

$$i = HHI = \sum_{j=1}^{N} s_j^2 \tag{1}$$

$$T_t, where\, t \in (2006, 2017)$$

Here i is an HHI-value in an ATC5-group$_i$, s_j is the market share of firm j in the market, N is the number of firms. Note column I is a set containing all elements of i for a year t.

Below we see a distribution of these HHI-values that are presented as a box plot. The box plot values are displayed as quartiles, with the median value being the line in the center of the box. The distribution of HHI-values decreases in both countries over time implying that the markets of off-patent medicines become more competitive over time. We see that in 2017 roughly 30% of the markets in Finland are still highly concentrated while there are practically no markets that are highly concentrated in Denmark i.e. have HHI-values of over 0.25. Interestingly we see no dramatic shift in market concentration after reference pricing was introduced in 2009, rather the persistent effect is an almost linear downward trend in the distribution.

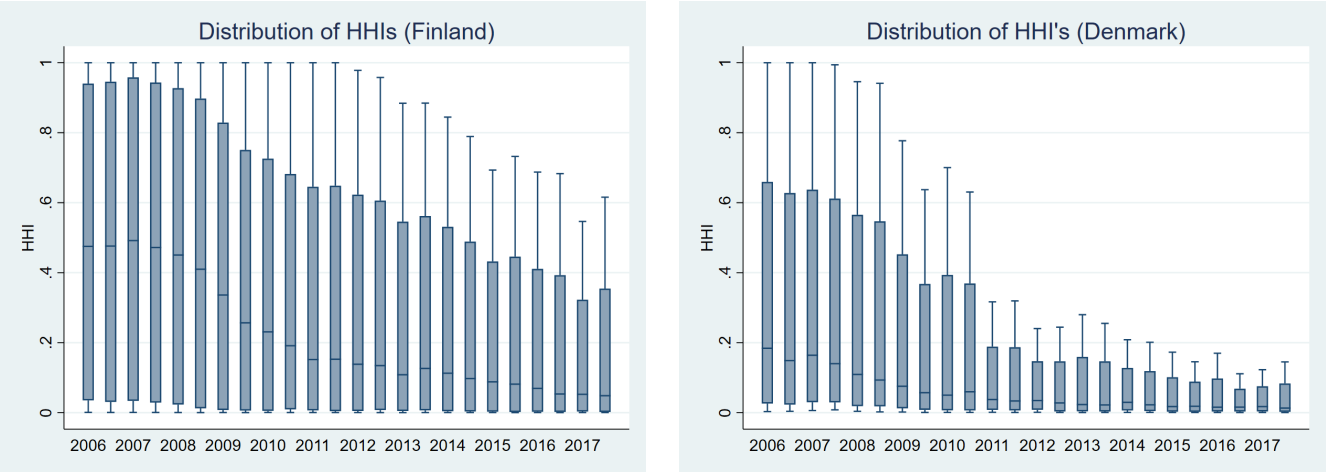


Figure 1: A comparison of the HHI's distributions

Previous literature finds that both highly concentrated markets and highly competitive markets decrease the probability of subsequent entry, generally finding a U-shaped relationship between market entry and market concentration (e.g. Amel

and Liang (1997), or Aghion, Bloom, Blundell, Griffith, and Howitt (2005)[19]). In addition, the use of market concentration as a tool in antitrust to measure market power can be criticized as the number of firms is also a function of demand conditions. Perhaps highly concentrated markets simply don't have enough demand to support the entry of a further firm resulting in more concentrated markets overall. Therefore, the implications that differences in market concentrations between Finland and Denmark will have on the empirical results is unclear.

Second, we want to look at how the market shares and revenue shares are distributed between different product types. A product can have one of three indicators: branded, generic or parallel import. I present the market shares and revenue shares of each type, without making any restrictions to the sample.

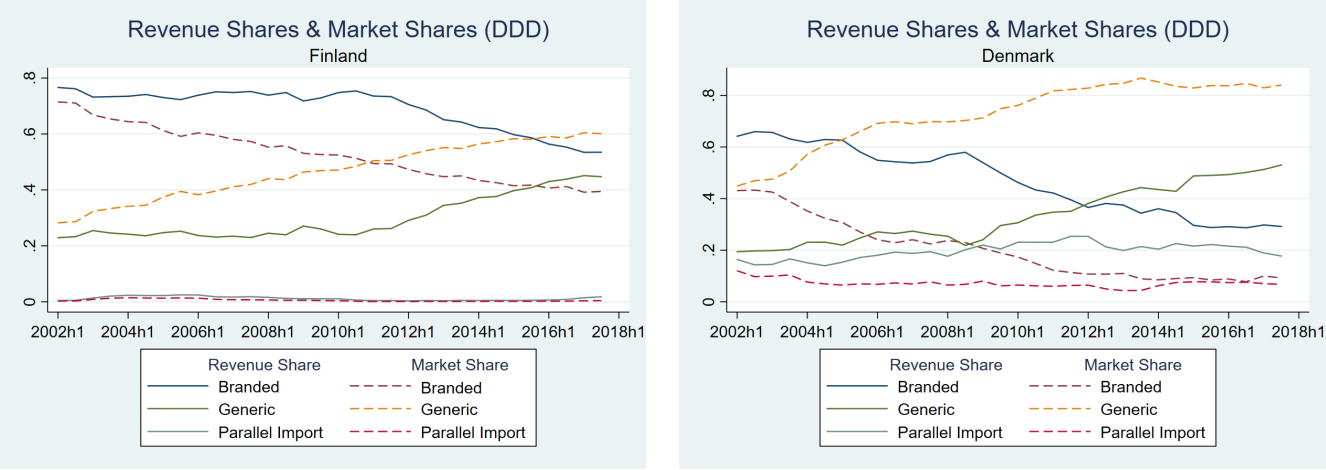


Figure 2: A comparison of the Revenue and Market Shares by firm type

Above we see a picture of revenue shares and market shares in Finland and Denmark. Revenue share is defined as the the total value of sales by package type.

[19] Aghion et al. study the relationship between competition and entry through innovation

The definition of market share that was used is congruous with the previous empirical pharmaceutical literature: Sales units are multiplied by the Defined Daily Dose in order to account for different product variations. The interpretation of the graph is invariant to this correction and defining sales volumes as units sold produced the same interpretation. A rudimentary separation into branded, generic and parallel imported products was made.

The immediate, striking observation is the difference in the level of parallel imported products in both countries. Parallel imported products have historically had roughly 20% of the market in Denmark, while their importance in Finland has been nominal over time. Another interesting finding is that revenue share is higher than market share for parallel imported products in Denmark, compare this to generic firms who have a larger market share than revenue share. As revenue share is calculated by adjusting for gross sales value, what this implies is that either the gross profit margins are larger for parallel imported products than for branded products or that parallel imported products on the whole are costlier medications. Both explanations are supported by earlier empirical findings: for instance Costa-Font (2016) found that parallel importing was largely effected by statutory distribution margins meaning that parallel importers seek products where there are the largest price differences and profit margins.

In Finland we see that revenue shares are higher for branded products than generic products, but this reverses if we look at market shares. The explanation for this is that branded products are able to charge higher prices than generic producers for the same products. We see an overall decline in the revenue shares of branded products in both countries which starts in 2008 in Denmark and 2010 in Finland. Though the levels of both revenue and market shares differ between the two countries, the overall trends are remarkably similar in that generic products

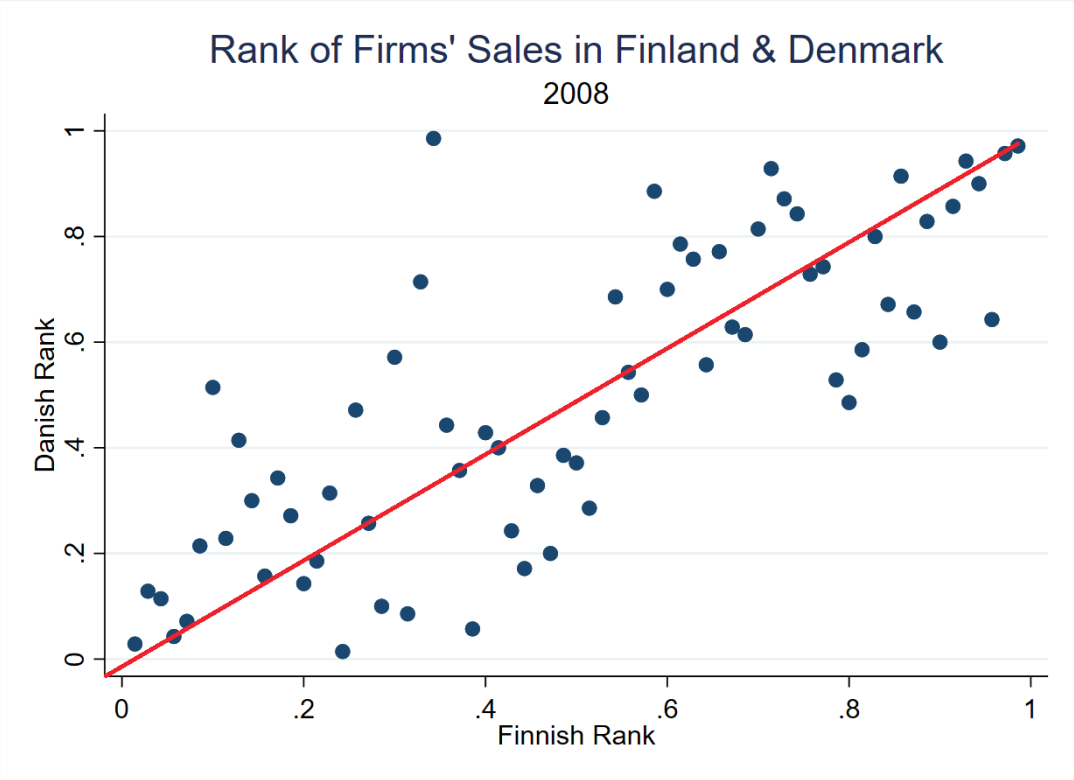
have increased their market share at the expense of branded products.

The final descriptive statistic concerns firm similarity between the countries. Do the same firms operate with the same intensity in both countries? Are the domestic markets dominated by local producers or are the same firms active in both countries? One measure of this is to calculate the sales volumes of firms that operate in both countries and rank them based on the size of sales. Note that this method only takes into consideration firms that are present in both countries and doesn't provide information on the firms that are only present in one country, which constitute around a quarter of the sample.

There are 70 firms present in both countries in 2008 and they are then ranked in terms of their net sales. The net sales are only calculated from ATC5-groups which were subject to the reference price reform in 2009. A more detailed description of the sample selection is provided in the data description section. The rank of the firms is then scaled from 0 to 1 so that 1 depicts the firm with the most sales and 0 the firm with the least amount of sales.

Below we see a snapshot of the ranking one period before reference pricing started in Finland:

Figure 3: The relative sizes of firms in Finland and Demnark



Note: The red line represents a 45-degree line drawn from the origin. Observations close to this line are firms that are relatively same sized in both Finland and Denmark

The closer an observation is to either axis, the smaller its' sales are in the other country. If the data points were bunched around a 45 degree angled line drawn from the origin then this would imply that in relative terms, firms would be the same size in both countries. We see some heterogeneity in the rankings. Something that stands out is one outlier that has almost a rank 1 in Denmark, but rank 0.4 in Finland. The outlier is a firm which focuses on parallel imports; a considerably more developed business in Denmark as we have previously learnt. No sweeping

conclusions on the similarity of the producers operating in both countries can be made based on this graph.

We can conclude that the types of products sold in both markets and by extension, the type of firms differ slightly between the two countries. Denmark has a larger share of parallel-imported products and the sales of branded products has experienced a sharper decline in the beginning of the century. Generic medicines account for nearly 80% of all units sold in Denmark in 2018, while they account for only 60% in Finland.

When considering causal inferences of market entry this could be slightly problematic as entry probability is affected by market size (Acemoglu and Linn (2004)), the number of available substitutes (Lu and Comanor (1998)) and is endogenous to the structure of the market. We don't know why the Danish market has more generic products or if this unobserved characteristic is correlated with future entry. I will control for country-specific heterogeneity by providing the same baseline regression results with Norway included as an additional control group. This will decrease the effect that Denmark-specific market characteristics unrelated to the Finnish policy reform have on the estimation results.

8 Data Description

I have used a compilation of data from multiple sources, each source is listed in the Appendix. The data was provided by VATT Institute for Economic Research, to whom I am extremely grateful. I observe package level sales volumes, prices, brand status, prescription status, market authorization holders etc. at a monthly level. The data contain all the aforementioned key variables from Finland, Denmark and Norway. I aggregate the data at a half year-level as both entry and exit are rare events. Though measuring the observations at a monthly level would provide more observations and choosing half years as the time unit is a somewhat arbitrary choice, I feel that I wouldn't be able to capture the effects of the policy on firm entry by using the monthly measures due to the large variation in firm entry/exit over months.

Unique firms are identified by name, which creates a problem as firms can have multiple legal affiliations and the cross-ownership of firms is not identified. A manual and automated process for deduplicating firm names was performed, described in more detail in the appendix. Unique products are easier to observe than firm names as they are identified by a Nordic Article Number henceforth known as the VNR-code. The VNR-code has six dimensions: package size, strength, dosage form, active ingredient, market authorization holder and the trade name. A change in any of the aforementioned identifiers would result in a new VNR-code and thus a new package. Despite what the name might suggest, the same VNR-code does not uniquely identify the product in all the Nordic countries, though it sporadically does so. This means that I am not able to reliably track the same package across countries, but I am able observe the sales of the same packages within a country with high precision.

I have selected ATC5-groups that were ever affected by the reference price reform as the market definition and will observe changes within those groups using the number of firms as the key dependent variable. Firms within the ATC5-groups in Denmark will act as the counterfactual for the Firms operating in Finland. These ATC5-groups are matched between the countries and I am able to perfectly observe ATC5-groups in both countries. Thus, a unique observation is a firm-country-halfyear-ATC5 observation. For some regressions I will add Norway as an additional control group to measure the robustness of the results.

I have imposed an additional restriction in that I have selected only ATC5-groups where generic substitution had started in Finland for at least one package within the group by 2007. This is because I want to isolate the effect of the reform by excluding drugs that lose their patent protection around 2009. Once a chemical ingredient loses its patent exclusivity, more often than not, generic producers will race to enter the market. As generic producers enter the market for the first time, the products will also likely be included in reference price groups for the first time. Thus, I would not be able to distinguish the effect of reference price policies on entry from the "natural" competition that arises after a product loses its patent exclusivity.

One might be concerned that including ATC5-categories that ever fall under reference pricing means the treatment group includes ATC5-categories that received only residual effects of the treatment or no treatment at all, i.e. those ATC5-groups that fall under the policy for the first time after 2009. One solution would be to only include ATC5-categories that immediately fell under reference pricing or to do an event study where time isn't measured in half years, but as periods before and after an ATC5-group falls under reference pricing. Both conditions carry their own limitations.

If we include ATC5-groups that were only subject to the reform immediately then we underestimate the true effects of the reform. We would omit groups that could've been subject to the reform immediately, as they operate in chemical substances that have lost their patent protection and that have generic substitution in place, but are not part of reference pricing in 2009. The legislation on reference groups is exhaustive and automatic from the regulators perspective, meaning that if the criterion of reference pricing are met, the regulator will create a reference group. Thus, it is a firm's choice to either belong in a reference group or to opt out of it, barring that the firm is a monopoly without any competition. The question is therefore why some off-patent ATC5-groups do not immediately fall under reference pricing? There is a clear endogeneity issue with the timing when an off-patent ATC5-group falls under reference pricing and unobserved ATC5-group qualities.

Transcribing time into event time, which in this case would be known as a staggered diff-in-diff or staggered adoption time, wouldn't solve this endogeneity issue. According to Athey and Imbens (2018), one formal assumption of a staggered diff-in-diff a model is that the timing of the treatment is as good as random and there is no anticipatory effect. It is a firm's choice to determine market participation at a given time which means that treatment (reference pricing) is not random. Thus, using a staggered approach would present it's own difficulties.

One consideration is how to treat OTC-drugs. The vast majority of OTC-drugs are not reimbursable and are therefore excluded from reference pricing. A valid strategy for a firm could be to opt out of reference pricing by not applying for a reimbursement status. In particular, for high volume, but cheap medications where price competition is fierce, this could be a valid strategy as applying for a reimbursement status is costly and relatively less valuable if most of the products sales would come from OTC-sales anyway. In this case we would simultaneously see

a decrease in the number of packages sold as prescription drugs and an increase in the OTC-sales, with an ambiguous total effect.

For some chemical ingredients, mainly pain medications, the weaker strengths of the drug are sold both as OTC-versions and prescription drugs whereas the stronger formulations are sold exclusively as prescription drugs. However, we have no reason to expect that firms would treat the markets separately, rather we'd expect firms to take both markets into consideration when deciding on entry and exit decisions. Therefore, dropping the OTC-market would underestimate the true impact of the policy reform. OTC-drugs are rarely directly affected by the reform, but they are indirectly affected by both the pricing of prescription drugs and as an extension, by the entry and exit rates of prescription packages. Therefore I have included OTC-drugs and their producers in the sample.[20]

As I have data on other Nordic countries as well, I will run additional regressions using Norway as a control group, for robustness sake, in order to control for country-specific shocks that occur in Denmark that are unrelated to the policy. Therefore, I will show in the descriptive statistics, data on the Norwegian market. However, I will not go into an in depth study on the Norwegian institutions for brevity's sake.

Here we see a sample descriptive statistics of key variables separated by country at two arbitrarily chosen years: 2008 and 2016.

[20] In my sample selection only 10 percent of the packages were OTC-drugs.

Table 2: Descriptive Statistics

	Total 2008			Sample 2008			Total 2016			Sample 2016		
	Fin	Den	Nor	Fin	Den	Nor	Fin	Den	Nor	Fin	Den	Nor
Number of Companies	213	217	230	109	121	105	222	219	247	112	132	104
Entries(Firm-ATC5)	147	198	128	76	110	45	166	253	98	73	92	25
Exits(Firm-ATC5)	91	143	106	45	66	50	162	263	86	57	119	35
Number of ATCs	1016	940	934	267	255	225	1135	1002	1039	262	255	224
Vnrs	6286	7004	3943	3660	4255	1896	7125	9193	3980	4114	5206	1778
Firm per ATC				5.77	6.87	3.66				5.55	8.61	3.65

9 Empirical Strategy and Identifying Assumptions

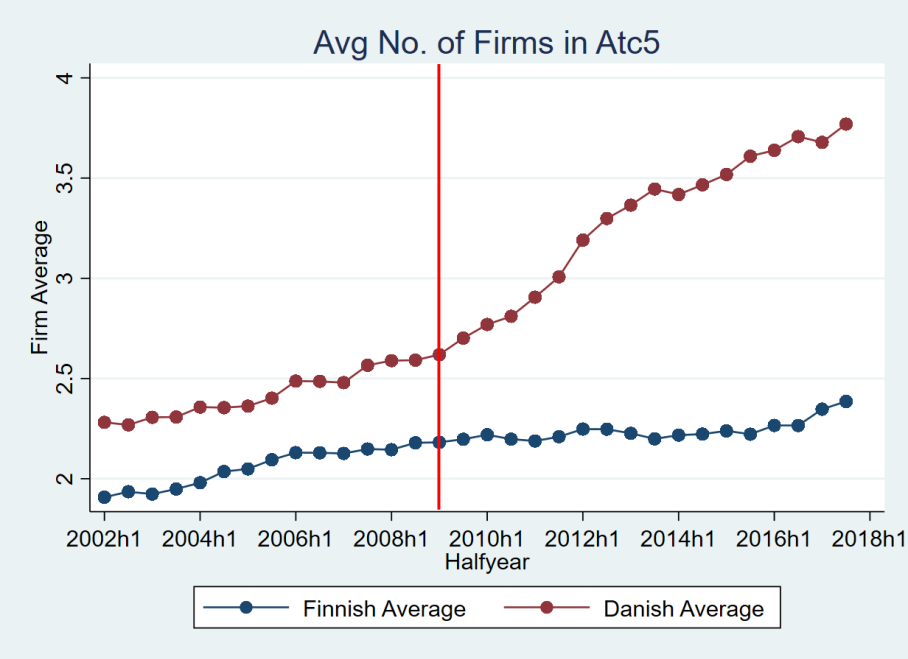
The principal empirical framework I will be using is a cross-country differences-in-differences regression, also called a diff-in-diff. The main identifying assumption of the diff-in-diff model is the parallel trends assumption, meaning that in absence of the treatment, the treatment and control group would've developed similarly. The parallel trends assumption implies that prior to the treatment, both the treatment and control groups grew at a similar rate, hence the name parallel trends.

The reason I expect the Danish market to be a good counterfactual for the Finnish market is because the institutional context is very similar between the countries. Both countries are Nordic welfare states that use roughly the same proportion (8-10%) of their GDP on health care expenditure. There are also multiple demographic similarities: Denmark has 5.77 million inhabitants, Finland has 5.5 million and both countries have an aging population (Eurostat (2015)).

We expect the countries to have roughly the same pool of prevalent diseases

and the "attractiveness" in terms of market size to be similar. The two countries need not be identical in the diff-in-diff setup, only that in absence of treatment the key dependent variable would've developed similarly which is indicated by the pre-treatment time-trends. Graphical indication of the parallel trends assumption in this case is the average number of firms in an ATC5-group which is presented below. More sophisticated regression post-estimation tests, namely Wald-tests, were also run in order to test the joint significance in pre-treatment trends for the treatment group.

Figure 4: The average number of firms in Finland and Denmark in an ATC5-group



Note: Beginning of treatment (2009 halfyear1) drawn in red

We see quite nicely from the graph that the average number of firms per ATC5-develops similarly prior to the treatment, which is indicated by the vertical red line. After the treatment the two trends start to deviate.

The other principal assumption in the diff-in-diff setup is the so-called Stable Unit Treatment Values Assumption (SUTVA) whereby the potential outcome of the control group is unaffected by results in the treatment group (Rubin (1977)). We assume that the cross-elasticities between the two countries are very small. To be more precise, the diff-in-diff assumptions are violated if the change in the Finnish reference price regulation affected the entry/exit decisions of Danish pharmaceutical producers. This assumption would also be violated if changes in i.e. Finnish exit rates affect Danish pharmaceutical firms decision to remain in the market at a later period or if firms would treat the Nordic market as one entity and would refrain from entering the entire market due to the new price control policies. In this case, the results would be biased and the model would underestimate the total effects of the reform.

Third, we assume that the timing of the policy is "As good as random", meaning that firms weren't able to anticipate the policy. If firms would manage to anticipate the effect, this would mean that part of the effect would be captured in the pre-treatment coefficients and some post-treatment coefficients could be biased. Parliamentary discussion of the policy began in 2008[21], while the policy itself was implemented in 2009, which could be a cause for concern. However, the processing time for market authorization applications can take up to 210 days. Thus, if there were firms in the process of entering in 2008, it is unclear whether they would have had time to react to the policy discussion. In any case, it is slightly unclear what

[21] Finnish Health Insurance Act, 802/2008

the precise time for the beginning of the policy should be. I have selected the half-year in which the policy was formally implemented (2009h1) as the beginning of the policy.

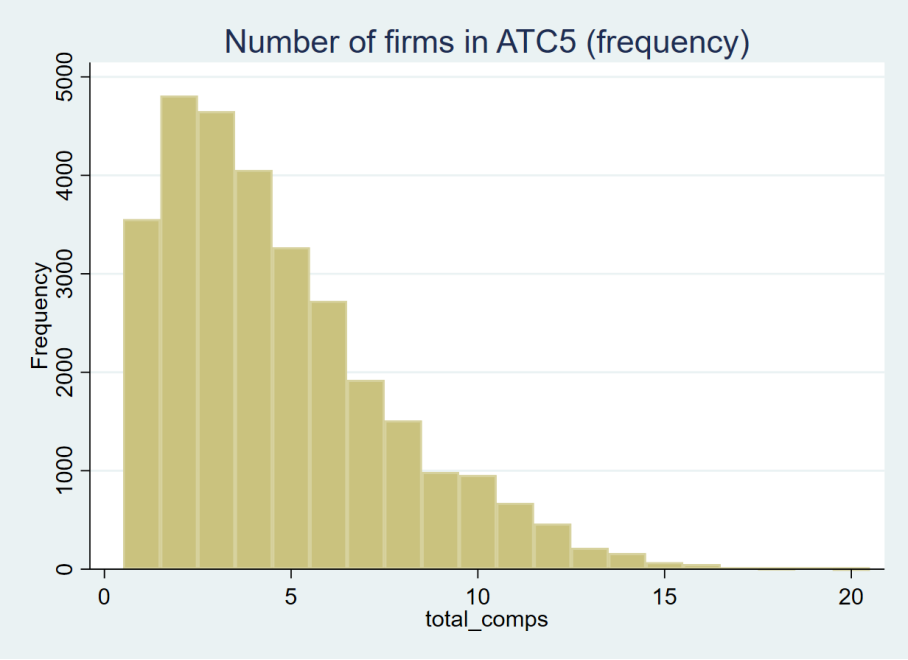
Finally, we assume that there are no other shocks that could uniquely affect either the treatment or the control group. The validity of this assumption is difficult to verify through any theoretical argument or empirical test as any domestic shock could potentially have an impact on pharmaceutical producers. I have identified three key shocks that could potentially violate the diff-in-diff set-up: in 2005 Denmark switched from an External Reference Price system to an Internal Reference Price system, and both in 2006 and 2013 Finland implemented mandatory cuts to pharmaceutical wholesale prices. The price cuts affected only prescription drugs in 2006 and were imposed on all pharmaceutical products in 2013. We may be concerned that these price control policies, in particular the earlier reforms could violate the diff-in-diff assumptions by having a residual effect on the estimate results. In light of this, the sample is chosen to include the years 2006-2011 to mitigate the long-run effect these simultaneous policies could have. I will run additional robustness checks by adding Norway as a control group in order to control for country-specific simultaneous shocks that might have occurred in Denmark.

We might also be worried that regulators would want to consciously incentivize price competition by creating a larger number reference price groups. Hila can influence reference pricing by granting a reimbursement status for a higher proportion of drugs as reference price groups can only be created from drugs that are reimbursable. From the data we observe that this is the case, as the number of packages receiving a positive reimbursement status for the first time grew from roughly 300 in 2008 to 500 in 2009. As a reimbursement status has a positive effect on sales, theoretically we should also see the number of entrants in a market increase.

10 Empirical Model and Results

The base model I present is how the number of firms develop in ATC5-groups. As the number of firms is by definition a non-negative integer value, the data is in the form of count data. The number of firms in an ATC5-group is heavily right-skewed and follows a Poisson distribution, as evident from the graph below. The graph depicts the number of firms per ATC5-group in the entire sample.

Figure 5: Histogram of firm-counts in sample



Note: This histogram includes the entire sample. This includes years from 2006-2012 and firm counts from a total of 266 ATC5-groups.

As the observations in a count data are typically bunched near 0 with no limiting upper-bound, the error terms rarely follow a normal distribution: by definition count data cannot have non-negative values and so the error terms for observations near zero could be biased (Cameron and Trivedi (2013)). As a result, using the standard linear Ordinary Least Squares (OLS) approximations are inadvisable. With count data the common solutions are then to use a Poisson regression or a negative binomial regression and estimation is done with maximum likelihood techniques (Cameron and Trivedi (2013)). The Poisson regression has a special property that unlike most non-linear models, it can be used in tandem with a fixed-effects model. This was originally demonstrated by Hausman, Hall, and Griliches (1984), who developed a generalized Poisson model in order to study the number of patents per firm based on R&D expenditures.

Using a fixed-effects regression I am able to control for differences in unobservable group-level shocks which greatly decreasing the probability of an omitted variable bias. I use ATC5-level fixed effects in order to account for potential shocks that affect different chemical ingredients. An additional benefit of the model selection is that the incidental parameters problem, where estimations with short panel data suffer an upward bias and which affects most non-linear regression models, is not an issue in fixed-effects Poisson models (Cameron and Trivedi (2013)).

A downside of the Poisson regression is that we impose an additional formal assumption for Poisson models whereby we assume that the mean must equal the variance (equidispersion property). If this is not the case, this is known as overdispersion and the model selection might not be justified (Cameron and Trivedi (2013)).

The formal equation of my base model is Equation (2):

$$E(Y_{cit}) = e^{(\alpha + \sum_{t=2007h1}^{2012h2} \beta_t D_{tc} + \mu_t + \mu_c + \mu_i)} \tag{2}$$

where the subscripts are c=country, i=ATC5-group and t=half-year and D is a dummy-variable that depicts the beginning of the policy. Note: The estimation period is the first half-year of 2007 until the second half-year of 2012 Hence:

$$D_{tc} = \begin{cases} 1, \text{ if t>2009h1 \& country=Finland} \\ 0, \text{ otherwise} \end{cases} \tag{3}$$

For brevity's sake, I only report the half-year*treated interaction terms and a country coefficient, which I report for some scope of magnitude. Half-year is annotated as h1; for instance the reform began in April 2009 which is depicted as 2009h1. Note, the base time-period to which all coefficients are compared to is 2008h2, which is omitted from the table as it's coefficient receives a value of 0 by definition. Pre-treatment trends were also included.

From Table 3 we see that country coefficients are statistically significant, which implies that in our sample, Denmark has more firms than both Finland and Norway. Only the first and last interaction terms are statistically significant at the 10 percent-level in our base-regression, though after the treatment starts in 2009h1 we see that all of the coefficients are negative. Ideally all pre-treatment coefficients would be statistically insignificant as this could suggest that there are no differences in trends between the two countries.

As virtually all of the coefficients are negative in the base regression once the policy begins in 2009h1, this would provide suggestive evidence that the number

Table 3: Main Regression(Firm Count)

	(1)	(2)
	Base	Controls
Finland	-0.181***	-0.198***
	(0.0359)	(0.0349)
Norway		-0.621***
		(0.0337)
2007h1*treated	0.0495*	0.0155
	(0.0249)	(0.0213)
2007h2*treated	0.0108	-0.00508
	(0.0212)	(0.0183)
2008h1*treated	-0.00454	-0.0176
	(0.0160)	(0.0137)
2009h1*treated	0.00111	0.00924
	(0.0173)	(0.0156)
2009h2*treated	-0.00860	0.00809
	(0.0240)	(0.0215)
2010h1*treated	-0.00502	0.0185
	(0.0258)	(0.0232)
2010h2*treated	0.000996	0.0195
	(0.0296)	(0.0269)
2011h1*treated	-0.0291	-0.00187
	(0.0312)	(0.0280)
2011h2*treated	-0.0320	0.000751
	(0.0340)	(0.0305)
2012h1*treated	-0.0398	0.00856
	(0.0368)	(0.0325)
2012h2*treated	-0.0857*	-0.0204
	(0.0395)	(0.0353)
Norway Included	No	Yes
N	6221	8875
ATC5-groups	266	266

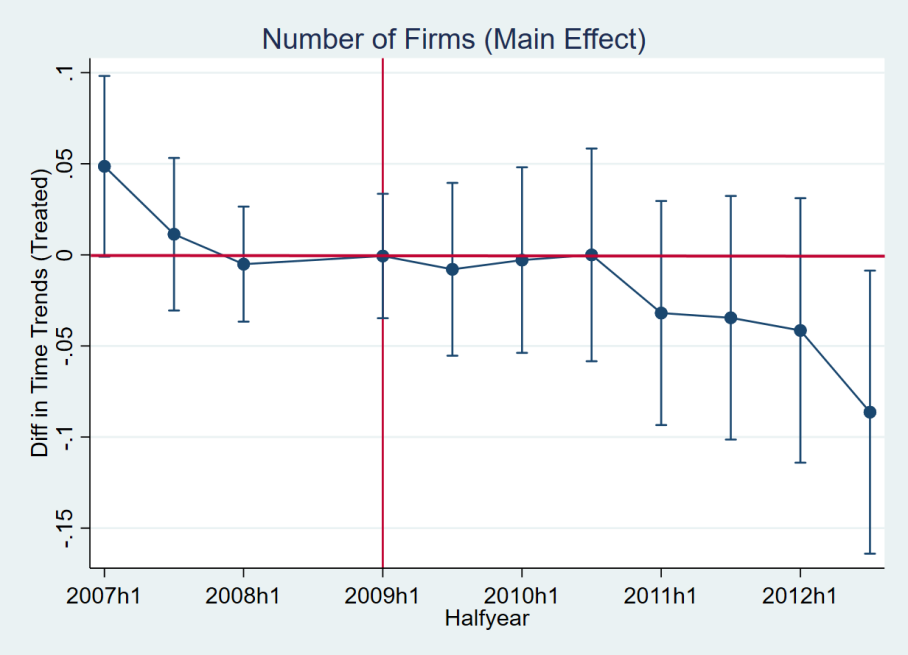
Standard errors in parentheses * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

of firms decreased after the policy reform, if not for the fact that the effect all but dissipates once Norway is added as an additional control. Once Norway is added, we see that the magnitude of the coefficients decrease and the interacted effects become non-existent.

Note that a Poisson regression's coefficients can be understood as percentages. For instance, the coefficient -0.0291 from 2011h1*treated implies that that number of Finnish companies decreased roughly 3 percent when compared to the number of Danish companies in the first biannual of 2011. The largest decrease occurred in 2012h2, when the number of Finnish firms grew -8.5% slower than in Denmark.

For a more visual representation of the base-line regression, we can show the marginal effects as a margins plot shown below.

Figure 6: Margins plot of main regression



To reiterate the margins plot depicts the interaction coefficients from the baseline

regression. The red vertical line is the beginning of the policy reform.

In order to test whether the interaction terms are jointly insignificant prior to the treatment, i.e. whether we accept that null-hypothesis that there weren't any differences in trends between the control and treatment groups prior to the treatment, a Wald-test was run. The Wald test's result was 0.0461 so we reject the Wald test's null hypothesis as $0.0461<0.05$. This means that we cannot reject the null hypothesis that there were differences in trends between Finland and Denmark prior to 2009 and therefore the robustness of the results isn't very high. This is exasperated by the fact that adding Norway into the control group completely changes the interpretation of the results.

In order to test whether the reform had heterogeneous effects by firm type a second regression was run. Here the original equation is slightly modified in order to include an index for firm type. Firm type $_{\text{f}}$ is very crudely defined as 1=Branded Firm, 2=Generic Firm, and 3=Parallel import firm. Firm type is calculated per ATC5-category, meaning that the same firm can have a number of different types over chemical substances. Firm type is measured by overall sales in an ATC5-category: if the majority of sales of a firm in an ATC5-group consists of Branded products, then the firm receives a typing of 1=Branded firm in that category.

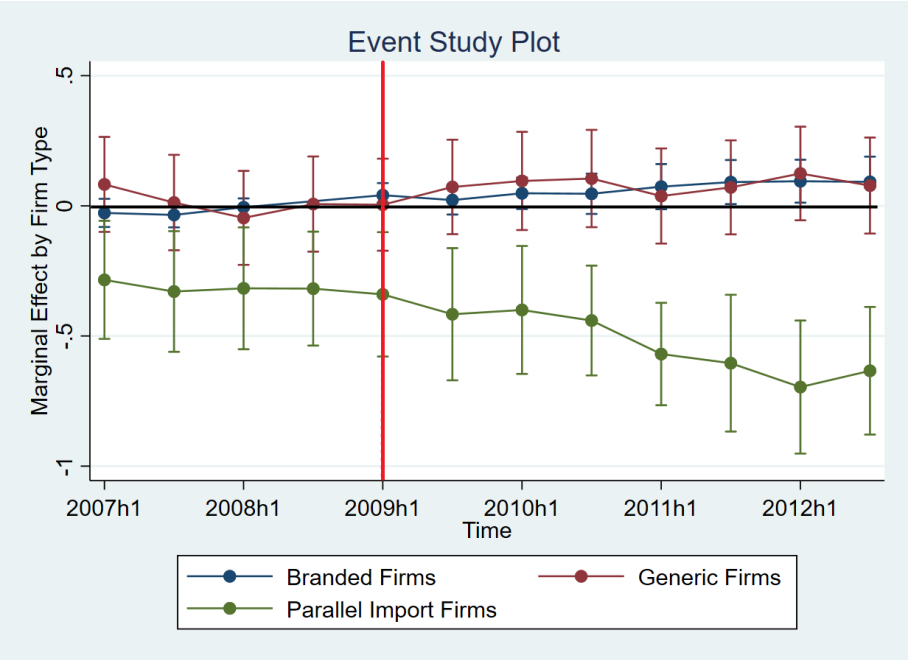
More formally:

$$E(Y_{citf}) = e^{(\alpha_f + \sum_{t=2007h1}^{2012h2} \beta_{tf} D_{tc} + \mu_{tf} + \mu_{cf} + \mu_{if})} \tag{4}$$

The first regression has been altered in order to include a firm-type dimension. Note: The statistical tool used for regressions (STATA) omits missing group observations from calculations.

Below we see a plot of the marginal effects:

Figure 7: Margins plot of firm-type regression



We see no statistically significant results for branded or generic firms. If anything, the results seem positive, though they are very close to zero. However, the most striking result is that the number of parallel imported firms has radically decreased over time in Finland, when comparing to the control groups. There are two likely candidate explanations for this: internal reference pricing affects parallel importing firms or Denmark is not a great control group for parallel importing firms.

Internal reference pricing can condense price differences as constrained consumers are incentivized to choose cheaper products and large deviations in prices can result in a radical decrease in revenue for the higher priced products. As prices condense, the possibility of arbitrage decreases and parallel importing firms will have fewer opportunities to find profitable markets. The alternative and more dejecting candi-

date explanation is that Denmark could be a poor control group. In the descriptive section I showed that the share of sales for parallel imported firms is roughly 20% in Denmark and only 2% in Finland and therefore the markets might not be comparable.

In any case, the number of parallel imported firms is significant prior to the beginning of the treatment, which suggests that the policy reform is not the only explanation for the differences between the treatment and control group. Running the Wald-test for each category separately we find that the joint hypothesis tests pass for generic and branded producers, but unsurprisingly fails for the parallel imported producers.

Finally we run a regression in order to test heterogeneous treatment effects across ATC1-categories. In order to ease interpretation I have run only an interaction with a dummy-variable that receives 1, if time is after the beginning of the policy 2009h1 and 0 otherwise. This is because there are 14 ATC1-categories and 12 half-year periods within the sample. If the regression would be run with half-year interactions, as the previous regressions were, this would yield 14*12=168 interaction coefficients to interpret.

More formally the equation is:

$$E(Y_{cit}) = e^{(\alpha+\beta*post*D+\sum_{i=2}^{14}\beta_i*post*D*M_i+\mu_t+\mu_c+\mu_i)} \quad (5)$$

Here:

i = ATC1-indicator

$Post = 1$ if the period is treatment, 0 otherwise

$D = 1$ if the market is a treatment market, 0 otherwise

$M_i = 1$ if market is i, 0 otherwise and i=2,3,...,14

Note that the market i=1 is the base-market to which all other markets are compared to.

We see only one significant category: Category P or Antiparasitic products. The interpretation of the coefficients is relative to the baseline, which is an arbitrarily chosen category: in this case ATC1-category A or alimentary tract medicines. The interpretation of the coefficients is that once the policy started in Finland the number of firms declined faster in group P than A at a 95 percent level. Note that Table 4 contains the saturated model, where each coefficient and their standard errors have already been compared to the baseline. There were two chemical ingredients within the Antiparasitic-group which was subject to the reform and therefore the interpretation of the results is somewhat redundant. For context, the median number of ATC5-ingredients per ATC1-category is 25 in the sample, with the largest category having 60 different chemical ingredients. The economic significance of this group is tiny compared with other ATC1-groups. No far-reaching conclusions about the impact of the reform across different ATC1-categories can therefore be made.

Table 4: ATC1 Heterogeneity Table, Marginal Effect

	(1)
Treatment*Treated	0.00320
	(0.0849)
Treatment*Treated*B	0.338
	(0.270)
Treatment*Treated*C	-0.0955
	(0.106)
Treatment*Treated*D	-0.112
	(0.134)
Treatment*Treated*G	-0.0452
	(0.130)
Treatment*Treated*H	0.235
	(0.176)
Treatment*Treated*J	-0.0540
	(0.120)
Treatment*Treated*L	0.118
	(0.128)
Treatment*Treated*M	-0.0219
	(0.122)
Treatment*Treated*N	-0.00774
	(0.104)
Treatment*Treated*P	-0.192*
	(0.0885)
Treatment*Treated*R	-0.150
	(0.145)
Treatment*Treated*S	0.303
	(0.172)
Treatment*Treated*V	0.0307
	(0.0885)
N	6221
ATC5-groups	266

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

11 Discussion

A key limitation of many earlier studies on reference pricing has been the lack of a credible control group. Some previous researchers have selected the control and treatment group exploiting the fact that not all chemical ingredients are impacted by reference price reforms (i.e. Brekke, Canta, and Straume (2016)). There are clear issues related to the fact that assignment into treatment and control groups is non-random in such a set-up and likely related to endogenous factors. Off-patent drugs omitted from reference pricing might not be comparable to drugs that are included in reference price groups. Recall that no reference group is formed if there is only one producer and this could be the case e.g. because the drug is sold in a declining market where entry is unfavorable, the drug is an orphan medicine that treats rare diseases and has only one producer, or competition may exist, but the national authority could've excluded the drug from drug substitution for various reasons. The SUTVA assumption in this set-up is also less credible as we expect firm entry in the treatment group to be affected by entry in the control group and vice-versa.

There are also numerous studies that use a before-and-after regression (see i.e. Koskinen, Ahola, Saastamoinen, Mikkola, and Martikainen (2014) or Rudholm (2001)). In these before-and-after studies no control group exists and the evidence is descriptive in nature as it is impossible to control for any time-variant shocks that simultaneously occur over the observations. As far as I am aware, this is the first cross-country difference-in-difference study used to estimate the effects of pharmaceutical reference pricing on generic entry. Even though there are limitations with this empirical design that prevent us from drawing causal inferences, that I have highlighted numerous times throughout this thesis, I find this empirical design to be a considerable improvement from earlier studies. This is because I am able to

perfectly match the exact same ATC5-groups in both the control and treatment group, which increases the credibility of the analysis as I am able to control for time-variant ATC5-level effects.

Previous research has found mixed results on the effects of reference pricing on competition and I add to this literature by finding further mixed results. I find only limited evidence that the reform had any negative effect on Finnish competition. Below I underline a few candidate explanations for why this might be the case.

1. The effect exists, but is too small to be captured

Firm entries and particularly firm exits from a chemical substance group are rare events and the data-set that contains firm-ATC5-halfyear combinations has roughly 3000 observations per country. The standard errors are in the scale of plus minus eight percent in the baseline firm regression that includes only Denmark as the control group. It is possible that there is a negative effect, but it falls within the bounds of the standard errors and we are therefore unable to infer statistically significant results. Recall that the coefficients for firm entry in the baseline regression were negative, which provides suggestive evidence that the true effect is negative for firms. There were also concurrent policy changes and some previous latent policy effects that were previously mentioned and that could have an impact on the estimation results, which would decrease our ability to capture the effect of the reference price reform.

Second, we need to be careful how we interpret the results, in particular how representative the number of firms is of "firm welfare". Previous empirical research finds that reference pricing decreases prices by anywhere from 6 percent to 30 percent (see i.e. Pavcnik (2002), Brekke et al. (2011), Kaiser et al. (2010)). This should reflect into firm profitability, which in turn will decrease the number of firms as the

theoretical literature a lá Bresnahan and Reiss might suggest. Exiting firms are those that found continued market participation to be unprofitable and were likely most affected by the reform, but they are hardly the only firms affected by the reform, as firms remain in the market whose profitability has drastically reduced. Perhaps a more holistic and more interesting proxy for "firm welfare" would be to study how firm profits developed as a result of the policy.

Naturally, the policy was not implemented with the goal of firm profit maximization in mind, it was aimed as a cost-containment policy. This thesis only provides suggestive evidence that there was a small negative effect on the number of firms, but is not able to answer how large on average this decrease in competition is on prices. For instance, Siikanen (2019) finds an initial decrease in wholesale prices, but a price rebound three years after the policy implementation and a possible explanation for this could be that the markets became more concentrated.

2. The effect exists, but only applies to some firms/markets

We could hypothesize that the average effect of the reforms was too small to be captured, but by firm type the reform had large effects. In particular, looking at the regression results we see that the baseline regression's negative yet insignificant results seem to be driven by parallel import firms. The effects were large in magnitude for parallel imported firms. This is intuitively a reasonable result: parallel imported firms benefit from price arbitrage. If a reform such as reference pricing condenses prices between producers, then there should be fewer opportunities for arbitrage especially since prices fall as a consequence of the reform.

However, previous empirical research such as Birg (2019) and Brekke, Holmås, and Straume (2015) has found mixed results on the impact of reference pricing on parallel imported firms. Birg finds that reference pricing increased the market

share of parallel imports by 75 to 85%, which is in stark contrast to my findings, whereas Brekke et al. found that a 10% decrease in a reference price resulted in a 5% reduction in the market share of parallel imported products.

Previous empirical and theoretical literature has also been ambiguous on the effects of reference pricing on branded producers. For instance Kaiser et al. (2010) finds a negative effect of reference pricing on branded firms. On the one hand, internal reference pricing should decrease the ability of incumbents to use market power such as their brand status in pricing and competition. On the other hand, the theoretical entry literature suggests that incumbent firms have lower fixed-costs than entrants, as they are already present in the market and don't need to pay entrance fees. On top of this, originator firms have had years to perfect their operations which might translate as lower average costs compared to potential entrants and incumbents could therefore pay to capture a larger portion of the market by investing into capacity. Finally, incumbent firms enjoy a first-mover advantage in pricing, meaning that they can use limit pricing to stave away potential competition. In any case this would mean that the incumbent originator firms would be well set up to face stronger price competition that would arise after the policy reform.

As a counterargument to the previous point, we concluded in the descriptive section that off-patent pharmaceutical markets have saturated and we have seen generic producers gain considerable market shares both in Finland and Denmark. This would contradict the previous hypothesis that branded firms would be better suited to face price competition in the off-patent market. In addition, this could be one candidate explanation why we don't see any marginal effect on branded firms: the dominant effect is the generification of the market, which has been particularly rapid in Denmark and thus we don't see the relatively small effect that Finnish price competition had on branded firms' exit.

3. The effect does not exist

Firm entry/exit is a radical response to market conditions while reference pricing is a non-restrictive policy that only indirectly affects competition through reimbursement rates. It is entirely possible that reference pricing and how it was implemented in Finland didn't affect firm behaviour in any way whatsoever or perhaps it did affect market structure, but any exiting firms were well replaced by price-competitive, generic firms that entered the market. In this case if we only study the number of firms, the total market equilibrium wouldn't change, but the characteristics of the firms participating in the market would change.

We might consider that the model choice or one of the numerous assumptions that have been imposed as a consequence of the empirical strategy prevent us from drawing causal inferences. The regression results provide only an interpretation of reality that is supplemented by the descriptive statistics and a contextual understanding of the industry and institutions. At it's core, the diff-in-diff model only captures market competition in a rudimentary before-and-after snap-shot from the market. It doesn't allow for higher-order dynamic modelling, where firm decisions are a response to their competitors decisions in previous periods. From this perspective, perhaps a dynamic structural model would the appropriate way to model this research question empirically.

12 Conclusions

In this thesis I have analyzed the competitive effects that the 2009 Finnish reference price reform had on market participants. Using Denmark as a control group I found only very limited evidence that the reform may have decreased the number of firms in Finland. After adding Norway as a control group the negative effect dissipated, suggesting that the results were not robust and possibly caused by Denmark-specific shocks rather than the Finnish reform. Looking at heterogeneous impacts of the reform by firm-type, we can conclude that there was no effect on branded or generic firm entry, but there was a large effect on parallel import firms.

The off-patent market for pharmaceuticals has experienced a strong shift towards towards generic products, with generic sales contributing roughly 80% of the market share in Denmark and 60% in Finland. This might in part explain why we saw no effect on the entry/exit of branded firms, as the dominant effect is a strong structural shift towards generic sales over time, which has occurred both in Finland and Denmark. The effects of the Finnish reform might be small in comparison and magnitude of the effect may be too small to be captured by my regression set-up.

Previous empirical evidence from reference price studies have found that pharmaceutical reference pricing decreases prices (Pavcnik (2002), Siikanen (2019), Koskinen (2018) and Matteo et al. (2011)). This price decrease theoretically constrains consumers so that the optimal price is on the elastic part of their demand curve, implying a decrease in firm profitability. Therefore, studying how firms respond to reference pricing is critical in understanding the total effects of the policy.

The likes of Brekke et al. (2011) and Kaiser et al. (2010) have found a negative effect on branded firms entry and sales after the implementation of reference pricing, which I do not document. Whether this is because the branded firms changed their

pricing policies, entry into the Finnish market is blockaded or the policy is too weak to be causally captured in my regression set-up remains an open-ended question.

I find that the pharmaceutical market is rich with opportunities to study using empirical industrial organization entry models. Many entry models require assumptions on for instance entry orders, which can quite trivially be solved in the pharmaceutical industry, where the first entrant is always a branded or originator drug and the second entrant is a generic entrant conditional that a parallel importer has not entered yet. Therefore, I find that future research could utilize i.e. Mazzeo's (2002) model in studying the competitive dynamics in the pharmaceutical market or could revolve around a more structural approach.

When studying the Finnish market, there is still the open-ended question how pharmacies respond to reference pricing. Pharmacies receive a higher mark-up for more expensive products, thus a valid strategy for pharmacies would be to stock only high-priced branded products and exclude a reference price group's cheaper package from their selection, which would dilute the intended effects of the reform. However, as far as I'm aware, this phenomenon has not been studied in detail and would present a great research opportunity, with heavy policy implications.

13 Appendix

13.1 Data Sources

Finnish Data on prices and quantities was provided by Fimea (Finnish Medicines Agency), the Association of Finnish Pharmacies and Lääketietokeskus. Additional supplementary material was gathered from Statistics Finland. The Danish Data was compiled by DLI-Market Intelligence and supplementary material was gathered from Statistics Denmark, namely on currency exchange rates. Norwegian data on prices and quantities was provided by Pharmastat.

I am extremely grateful for VATT Insitute of Economic Research for providing the data and offering the resources needed to complete this thesis. This thesis was completed in tandem with VATT's and Aalto Universities joint research project on the Fiscal Expenditure of Pharmaceuticals.

13.2 Firm Names

Firm names have been manually processed and filtered. This is because a firm can have multiple legal affiliations and international companies have subsidiaries and licensees overseas. Some firms have chosen to separate different departments and research facilities into separate legal entities, which inflates the number of occurrences a firm is registered in the data. Furthermore, there are slight variations on how corporate names are spelt within the data set, thus uniquely identifying a firm presents a challenge. The goal of filtering firm names is to create one unique name that correctly identifies the same corporation across all countries.

The filtration was done in two ways, one was to painstakingly go through all observations, roughly 2000 unique firm names and replace the obvious duplicates

with one key name. In case of any uncertainty, more information relating to historic names and M&A's was sought online. The other method was to loop across observations and keep only the shortest version of the name in the data-set, again with some manual processing required. The final product was roughly the same in both cases: the number of truly unique names dropped by around 33 percent in the data, with no variation across countries. I would like to especially thank civil servant Jaakko Markkanen for his aide in this process.

Glossary

Anatomic Therapeutic Classification (ATC) System

A system that classifies drugs based on their therapeutic and pharmacological properties as well as by their active ingredients. There are five levels, at which the drugs are classified. The system is controlled by the World Health Organization.

branded drug

See originator drug.

European Medicines Agency (EMA)

A centralized European agency that oversees the evaluation and supervision of medical products. The European Medicines Agency was founded in 1995 under the European Unions jurisdiction.

External Reference Price System (ERP)

A price control mechanism where the maximum reimbursement of a pharmaceutical product is determined by the prices of external countries.

G-Scheme

A voluntary generic drug substitution programme adopted by Denmark in 1991. The programme received it's name from doctors who would write a small g on prescriptions where drug substitution was allowed.

generic drug

A drug that was not the original patent holder of a chemical ingredient but contains the same active ingredient as the originator.

generic substitution

A policy which aims to increase the uptake of generic drugs by pooling similar drugs into substitution groups and imposing restrictions on doctors/pharmacies to prescribe and sell the cheapest versions of substitutable drugs.

Informal Reference Pricing

A reference price system that does not strictly control domestic pharmaceutical prices through i.e. average drug prices, rather uses external prices as a benchmark.

Internal Reference Price System (IRP)

A reference price system where the maximum reimbursement is set by the domestic, minimum price in a pool of similar drugs.

originator drug

The drug that was the initial patent holder of a chemical ingredient. In some contexts might be called a "branded" drug.

Over-The-Counter (OTC) drugs

Drugs that can be bought without a prescription.

parallel import

A drug purchased from a European wholesaler by a firm that does not hold the patent for a drug, which is then imported from a high-priced country and sold at a lower priced country. Parallel importers exploit opportunities of arbitrage that arise from price differences between European countries.

The Danish Association of the Pharmaceutical Industry (Lif)

A Danish trade organization that represents the interests for the researching pharmaceutical industry.

The Pharmaceutical Pricing Board (Hila)

The pharmaceutical pricing board is in charge of constructing reference price groups. The pharmaceutical pricing board also negotiates with pharmaceutical firms on wholesale prices for products under the Finnish reimbursement scheme.

The Social Insurance Institution (Kela)

A Finnish organization that is in charge of Finnish benefit schemes and handling reimbursements for pharmaceutical products.

therapeutic substitution

Drug substitution that occurs between drugs that do not have the same active ingredient, but are used to treat the same symptoms or diseases.

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